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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,315	10/29/2001	Robert V. Farese JR.	UCAL-105CIP2	1732

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,315	FARESE ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-21 and 66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17,19-21 and 66* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/01,9/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/20/2006 has been entered.

Applicant's cancellation of claims 1-14 and 22-29 and the amendment of claim 15, in the paper of 11/23/2005, is acknowledged. Claims 15-21 and 66 are still at issue and are present for examination.

Applicants' arguments filed on 11/23/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The disclosure is objected to because of the following informalities: Applicants previous arguments have raised a question as to whether the current SEQ ID NO: 10 listed is a plant amino acid sequence, as applicants argue in their previous response, or whether it is a mouse amino acid sequence as it is listed in the sequence descriptor.

Appropriate correction or clarification is required.

Claim Objections

Claim 18 are objected to because of the following informalities:

Claim 18 is dependent on rejected claim 15.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-17 and 19-21 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a screening assay for determining a candidate agent's DGAT modulatory activity, comprising contacting a DGAT polypeptide having the amino acid sequence of SEQ ID NO: 6, with said candidate agent and detecting a change in diacylglycerol-O-acyltransferase activity of said DGAT polypeptide compared to a control to determine said candidate agent's DGAT modulatory activity, does not reasonably provide enablement for any screening assay for determining a candidate agent's DGAT modulatory activity, comprising contacting a DGAT polypeptide, having a mere 90% amino acid sequence identity to the amino acid sequence of SEQ ID NO: 6, with said candidate agent and detecting any change in activity of said DGAT polypeptide compared to a control to determine said candidate agent's DGAT modulatory activity. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was made in the previous office action as it applied to previous claims 15-17, 19-21 and 66. In response to this rejection applicants amended claims 15 and traversed the rejection as it applies to the newly amended claims.

Applicants continue to traverse the rejection made previously on the basis that applicants specification describes a number of species of DGAT polypeptides, including human DGAT (SEQ ID NO: 6), mouse DGAT (SEQ ID NO: 7) and a plant DGAT (SEQ ID NO: 10). It is noted that applicants reference to the "plant amino acid sequence" of SEQ ID NO: 10 is confusing as SEQ ID NO: 10 is listed in applicants sequence listing as a mouse sequence, not a plant sequence.

Applicants further submit that applicants teach how to determine whether an agent modulates DGAT activity as well as working examples. Thus applicants conclude given this guidance combined with the skill in the art those skilled in the art could carry out the claimed screening assay without undue experimentation.

Applicants further submit that applicants discusses structural features of DGAT polypeptides, such as a serine residue which is also found in acylCoA:cholsesterol acyl transferase (ACAT), hydrophobic domains and about 9 transmembrane domains.

Applicants further submit that those skilled in the art could readily identify conserved residues and domains using standard alignment software, such as the conserved serine residue and conserved arginine clusters.

Applicants thus conclude that because the instant specification teaches how to make and use the instant screening methods as claimed, one of ordinary skill in the art could readily practice the claimed invention without undue experimentation.

Applicants complete argument has been considered, however, continues found nonpersuasive for the reasons previously made of record and on the basis that while applicants have provided a few (two or three?) species of DGAT polypeptides that may be used in the claimed screening assay as well as direction in determining whether an agent modulates diacylglycerol-O-acyltransferase activity, this amount of guidance is insufficient to enable the claimed genus of screening assays that encompass the use of any DGAT polypeptide having a mere 90% amino acid sequence identity to SEQ ID NO: 6 comprising detecting "any change in activity" of said DGAT polypeptide. It is not persuasive that applicants teaching of "how to determine DGAT activity" sufficiently enables how to detect "any change in activity" of a DGAT polypeptide. Such a "detection step" is read as broadly as is reasonable, and is thus read as detecting any change in any activity of a DGAT polypeptide. Such includes activities in addition to enzymatic activity, such as regulatory, biological, immunological and transcriptional activities, etc... While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, the variants encompassed by applicants claims (i.e., 90% identical to the DGAT polypeptide of SEQ ID NO: 6) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the near infinite number of variants have the necessary property. Without such guidance one of ordinary skill would be

reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. While applicants have pointed out some structural consistencies between the reported polypeptides (i.e. conserved serine residue, hydrophobic domains and transmembrane domains), these are insufficient to enable the breadth of the claimed genus of methods.

As previously stated the specification insufficiently establishes: (A) regions of the protein structure of DGAT which may be modified without effecting DGAT activity; (B) the general tolerance of DGAT polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a DGAT with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the activity necessary to practice the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would continue to require undue experimentation for one skilled in the art to arrive at the majority of those methods of use of those DGAT polypeptide of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any screening assay for determining a candidate agent's DGAT modulatory activity, comprising contacting any DGAT polypeptide, having a mere 90% sequence identity to SEQ ID NO: 6, with said candidate agent and detecting "any change in activity" of said DGAT polypeptide compared to a control to determine said candidate agent's DGAT modulatory activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

Rgh
12/28/2004